UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,281	06/09/2005	Jean-Christophe Leroux	37991-0033	4230

21839 7590 10/19/2007
BUCHANAN, INGERSOLL & ROONEY PC
POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER	
SASAN, ARADHANA	
ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
10/19/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com
debra.hawkins@bipc.com

Office Action Summary	Application No.	Applicant(s)	
	10/507,281	LEROUX ET AL.	
	Examiner	Art Unit	
	Aradhana Sasan	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-16,20,21,23 and 26-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-16,20,21,23 and 26-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/9/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Applicant's remarks regarding the allowed claims of copending application 10/647,243 filed on 07/14/2006 are acknowledged. However, a search was conducted on the instant claims and an office action on merit follows.

2. Claims 1, 3-16, 20-21, 23, 26-35 are included in the prosecution.

Priority

3. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d).

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on 06/09/2005 was filed. The submission is in compliance with the provisions of 37 CFR 1.97 and 1.98. Accordingly, the examiner is considering the information disclosure statement. See attached copy of PTO-1449.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1, 3-16, 20-21, 23, 26-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fanara et al. (US 6,464,987) in view of Luo et al. (Chem. Commun., 2001, 1556-1557).

The claimed invention is a heat-sensitive composition in liquid form, comprising a hydrophobic organic liquid, an organogelling substance, and a bioactive substance. The composition changes to the organogel form during its administration to an animal body.

Fanara teaches pharmaceutical compositions which allow the sustained release of at least one active substance, to methods for preparing these compositions, as well as to their use for administering medicinal products subcutaneously and/or intramuscularly (Col. 1, lines 6-10). "The compositions have the property of gelling instantaneously in the presence of an aqueous phase ... upon contact with mucous membranes, a gel forms under the skin or in the muscle, and the medicinal product may diffuse and be released from the gel" (Col. 1, line 65 to Col. 2, line 5). The composition comprises: "a) a therapeutically effective amount of at least one active substance, b) from 3 to 55% by weight of phospholipid, c) from 16 to 72% by weight of pharmaceutically acceptable solvent, and d) from 4 to 52% by weight of fatty acid" (Col. 3, lines 25-35). Active substances include antibiotics, anti-inflammatory agents, peptide active substances such as calcitonin, somatostatin, insulin, bone growth hormone and other growth or repair factors (Col. 3, lines 42-65). The compositions are "fluid pharmaceutical compositions which are in the form of emulsions, suspensions or oily preparations" (Col. 5, lines 18-20).

Fanara does not expressly teach alanine as an organogelling substance.

Luo teaches self-assembled organogels formed by mono-chain L-alanine derivatives. Stable organogels were formed by mixing an L-alanine derivative with an organic liquid (Page 1556, left hand column). Luo teaches that intermolecular hydrogen

bonds are formed into a hydrogen bond network (Page 1556, right hand column). "Simple mono-chain L-alanine derivative can self-assemble into bilayer aggregates through intermolecular hydrogen bonding and the homochiral effect in a number of organic liquids, which are juxtaposed and interlocked by van der Waals interaction, and finally gelate the organic liquids" (Page 1557, right hand column).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition that gels instantaneously in the presence of an aqueous phase, upon contact with mucous membranes, as suggested by Fanara, and combine it with the self-assembled organogels formed by mono-chain L-alanine derivatives, as suggested by Luo, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Luo teaches that the organogels that are formed by mixing an L-alanine derivative with an organic liquid are stable. This confers an additional advantage to the sustained release formulation that may be subcutaneously and/or intramuscularly administered (as taught by Fanara).

Regarding instant claim 1, the limitation of a heat-sensitive composition would have been obvious to one skilled in the art over the teaching by Fanara that the compositions gel upon contact with mucous membranes (a gel forms under the skin or in the muscle). The limitation of a composition in liquid form would have been obvious over the fluid compositions taught by Fanara. The limitation of a hydrophobic organic liquid would have been obvious over the phospholipids (including Phosal 50 PG™ that contains phosphatidylcholine, soybean fatty acids, sunflower monoglycerides, ethanol,

propylene glycol and ascorbyl palmitate) taught by Fanara (Col. 5, lines 56-59). The limitation of the organogelling substance, the molecules of which have the capacity to bind together via bonds of low energy would have been obvious over the teaching of self-assembled organogels formed by mono-chain L-alanine derivatives, and of intermolecular hydrogen bonds and van der Waals interactions leading to gelation by Luo. The limitation of the bioactive substance would have been obvious over the active substance taught by Fanara.

Regarding instant claim 3, the limitation of a hydrophilic organic solvent capable of creating weak bonds with the organogelling substance would have been obvious to one skilled in the art over the ethanol in Phosal 50 PG™ taught by Fanara.

Regarding instant claims 4-5, the limitation of the organogel having a transition temperature from the liquid state to the gel state which is lower than the temperature of the site of application, and a transition temperature from the gel state to the liquid state that is higher than the body temperature would have been obvious to one skilled in the art over the teaching of a fluid composition that gels under the skin or muscle for sustained release of an active substance as taught by Fanara. This is because a liquid composition in order to gel under the skin or muscle would intrinsically have a transition temperature (from liquid state to gel state) lower than the temperature of the site of application. Also, a gel that was implanted in the skin, in order to release an active substance in a sustained or controlled manner, would intrinsically have a transition temperature (from gel state to liquid state) higher than the body temperature, otherwise

there would be dose dumping of the active and not the sustained release disclosed by Fanara.

Regarding instant claims 6 and 26, the limitation of the proportion of the hydrophilic organic solvent would have been obvious to one skilled in the art over the 1.03% ethanol (1. 9% ethanol x 54.6%Phosal 50 PG™) as taught by Fanara (Col. 6, Table 1).

Regarding instant claims 7-8, the limitation of the hydrophilic organic solvent would have been obvious to one skilled in the art over the ethanol and propylene glycol (Col. 5, line 61) taught by Fanara.

Regarding instant claims 9-12, and 27, the limitation of the hydrophobic organic liquid would have been obvious to one skilled in the art over the soybean fatty acids and sunflower monoglycerides taught by Fanara. One skilled in the art would use different organic liquids or a mixture of different organic liquids during the process of routine experimentation in order to optimize the stability and release profile of the composition and the recited hydrophobic organic liquids would have been obvious variants unless there is evidence of criticality or unexpected results.

Regarding instant claims 13-14, the limitation of the biologically active substance would have been obvious to one skilled in the art over the peptide active substances such as calcitonin, somatostatin, insulin, and bone growth hormone taught by Fanara.

Regarding instant claim 15, the limitation of the percentage of organogelling substance would have been obvious to one skilled in the art over the 3 to 55% by weight of phospholipid taught by Fanara.

Regarding instant claims 16, and 28-31, the limitation of the organogelling substance as a molecule of low molecular weight would have been obvious to one skilled in the art over the organogelling alanine derivatives taught by Luo. The recited alanine ester derivatives would have been obvious variants to one skilled in the art during the process of routine optimization.

Regarding instant claim 20, the limitation of an organogel remaining stable in gelled form would have been obvious to one skilled in the art over the gelling composition taught by Fanara, in view of the stable organogelling alanine derivatives taught by Luo.

Regarding instant claims 21 and 32-35, the limitation of a method for administering a bioactive substance to an animal would have been obvious to one skilled in the art over the composition where a gel forms under the skin or in the muscle taught by Fanara.

Regarding instant claim 23, the limitation of a process for preparing a composition would have been obvious to one skilled in the art over the method for preparing a composition where a gel forms under the skin taught by Fanara (Col. 5, lines 29-47).

Conclusion

7. No claims are allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MPW

MICHAEL P. WOODWARD
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600